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Hpv Type Distribution In New Haven County, Ct Among Women With Cin2+ Diagnoses From 2008-2010

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Abstract

Background

The human papillomavirus is a necessary cause of cervical cancer leading to >12,000 cervical cancer diagnoses and >4,000 deaths in the United States in 2007. In 2006, the first HPV vaccine was approved by the US FDA, which prevents the acquisition of high-risk types of HPV (16/18) that cause 70% cervical cancer cases in the US and 50% of precancerous lesions. Our objectives were to examine HPV type distribution among women with cervical intraepithelial neoplasia 2/3 (CIN2+) by area-based measures of race, ethnicity, and poverty and individual level characteristics.

Methods

In 2008, the Connecticut Department of Public Health (DPH) mandated reporting of CIN2+. Diagnostic specimens from women aged 18–39 years residing in New Haven County and reported during 2008–2010 were sent to the CDC to ascertain HPV type(s) which were subsequently coded as vaccine type (16/18 with or without other HPV types) or non-vaccine type (all others). Cases were also geocoded to census tracts (neighborhood level) and linked to measures of percent of the population living below the federal poverty level, proportion of population Hispanic, and proportion of population black. Statistical analyses included chi-square tests, logistic regression, and generalized estimating equations.

Results

Our sample consisted of 917 women who had HPV typing data available. Among these women, 41.9% had an HPV type (16 or 18) that is covered by the vaccine. In areas where 20% or greater of the population is living below poverty level, a significantly higher proportion of women had non-vaccine type HPV (60%) compared to women living in areas where less than 5% of women lived below poverty (50.5%%, p=0.05). Individual race/ethnicity analysis shows that black and Hispanic women were more likely to have non-vaccine type HPV (63.8% and 61.2% respectively). Analysis by area-based race and ethnicity showed that women who live in areas with higher proportions of black or Hispanic populations had higher proportions of non-vaccine type HPV. Specific non-vaccine HPV types were more prevalent in non-Hispanic blacks and Hispanics compared to non-Hispanic whites. Some main types included 35, 52, and 58 that together accounted for 35.8% of the HPV found among black women, 23.3% of HPV among Hispanic women and only 14.8% of HPV among white women.

Conclusions

Area-based results showed that women who live in areas with higher proportions of the population black, Hispanic or living below poverty have higher percentages of non-vaccine type HPV than vaccine type HPV (16/18). Similarly for individual level characteristics, non-Hispanic black and Hispanic women were also more likely to have non-vaccine type HPV compared to white women. HPV types not included in the current vaccines are causing a significant amount of precancerous lesion morbidity among minority women. These baseline differences need to be taken into account when evaluating the impact of the current HPV vaccines and when considering the development of future multi-valent HPV vaccines.

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Introduction

HPV Epidemiology and Background

Genital human papillomavirus (HPV) is the most common sexually transmitted infection (STI) in the United States and is the necessary cause of cervical cancer and precancerous cervical lesions. In the United States, it is estimated that 20 million people have genital HPV currently with 6 million new infections occurring every year [1]. There are more than 100 types of HPV with 40 types that are sexually transmissible. Genital HPV prevalence rates range from 27 to almost 45 percent with the highest prevalence rates found in females aged 20 to 24 years [2]. It is also estimated that nearly 80% of all people who have ever been sexually active have had one or more HPV types in their lifetime [1].

In the U.S. in 2004, there were an estimated 12,000 incident cases of cervical cancer and 3,850 attributable deaths [3] even though mortality due to cervical cancer is largely preventable in the U.S. due to the availability of routine screening and proper treatment [4]. High-risk and low-risk HPV types are categorized depending on their association with different disease outcomes including cervical cancer. Persistent infection with high-risk HPV types 16 and 18 cause approximately 70% of cervical cancer cases [5] and 50% of cervical precancerous lesions worldwide [6]. However, there are 12 other HPV types that the International Agency for Research on Cancer (IARC) deems carcinogenic [7, 8]. These types include HPV-31, -33, -35, -39, -45, -51, -52, -56, -58, -59, -66, and -68, however, their respective prevalence in precancerous lesions has not been completely determined [9]. Low risk HPV includes non-oncogenic types, such as 6 and 11 that are responsible for genital warts [5].

HPV Vaccines

In June 2006, the U.S. Food and Drug Administration (FDA) approved the first prophylactic HPV vaccine that protects against HPV types 6, 11, 16, and 18 [10]. Three years later the FDA approved the second vaccine, which protects against the two most common carcinogenic types, 16 and 18 [11]. Both vaccines have very high levels of efficacy and have the potential to reduce cervical cancer and precancerous lesion incidence as shown by early evidence from Australia's intensive HPV vaccination program [12]. Australia was the first country to implement a universal free HPV vaccination program for all females aged 12-26 using the quadrivalent vaccine and a recent study done shows the program's early successes. The study results show a small yet significant decrease in incidence of high-grade cervical abnormalities in girls younger than 18 years within the first 3 years of the program suggesting the impact that the vaccine can have when given as recommended to young girls before they become sexually active [12]. Currently, a new 9-valent HPV vaccine developed by Merck is in phase III of trials although no definitive results have been released. According to Merck's website, they plan to apply for a Biologic License Application (BLA) in 2012 suggesting that the phase III trials have produced favorable results[13].

Cervical Cancer Disparities in The United States

Women who live in poverty and who are racial and/or ethnic minorities have higher rates of cervical cancer morbidity and mortality [14]. Over the years these rates have decreased due to increased screening coverage [3], however non-Hispanic black and Hispanic women still have a higher morbidity and mortality burden than do non-Hispanic white women. Data collected in the United Sates from 1992-2003 show that Hispanic women had the highest incidence of cervical

cancer overall (24.2/100,000) as well as the highest incidence of the two most common histologic types of cervical cancer, squamous cell carcinoma (18.3/100,000) and adenocarcinoma (4.6/100,000) [15]. Non-Hispanic black women have the second highest overall cervical cancer incidence (16.3/100,000) and squamous cell carcinoma incidence (12.6/100,000), while non-Hispanic white women had the lowest overall cervical cancer (10.8/100,000) and squamous cell carcinoma incidence (7.2/100,000) [15]. Furthermore, it has been shown that women who live in lower socioeconomic areas have higher rates of late stage cancer diagnoses and lower survival rates compared to women in high socioeconomic areas [14]. However, data from 1975-2000 do show that the gap between low and high SES women for incidence of cervical cancer and related mortalities may be decreasing [14]. Nevertheless, there is a clear racial, ethnic, and socioeconomic disparity that exists in cervical cancer incidence and mortality [15]. Furthermore, research shows that vaccination completion rates among minority women are lower than non-minorities, possibly leaving these women more susceptible to the HPV types responsible for the majority of cervical cancer cases[16].

Very few studies done in the United States have described HPV type distribution in precancerous CIN2+ lesions among women of different racial and ethnic backgrounds. Guan et al. give the most comprehensive look at HPV types found in CIN2+ lesions worldwide, although they presented differences on a continent-wide macro scale rather than an individual race/ethnicity micro scale [6]. Furthermore, little information exists linking census tract area-based measures of race, ethnicity, and socioeconomic status to the type distribution of HPV. The use of census tract-level measures to assess and monitor socioeconomic (SES) inequalities has shown to be a rigorous and accurate way of measuring health disparities in the United States [17]. The objective of this analysis is to examine HPV type distribution among women in New

Haven County (NHC) who have a reported diagnosis of cervical intraepithelial neoplasia 2/3 (CIN 2+) by area-based measures of race, ethnicity, and poverty as well as by individual level sociodemographic characteristics including age and health insurance.

Methods

Surveillance for CIN2+/AIS in New Haven County, CT

The HPV-IMPACT monitoring system was established in 2008 and is a collaboration between the Centers for Disease Control (CDC) and five sites of the Emerging Infections Program (EIP) with the purpose of monitoring the impact of the HPV vaccines on CIN2+ lesions. Connecticut is one of 5 EIP sites and collects data through statewide passive surveillance for CIN2+ diagnosis from the 34 pathology labs that exist in Connecticut. In CT on January 1, 2008 CIN2+ and adenocarcinoma in situ (AIS) were added to the list of mandatory reportable conditions. Reports include diagnostic information as well as patient demographic information. In addition to statewide surveillance, enhanced surveillance in the New Haven County (NHC) catchment area for women aged 18-39 years is conducted and includes medical chart reviews and phone interviews to gain additional information including demographic information that is often missing on pathology reports. Interview demographic data is considered the most accurate source of demographic information but not all women can be reached by telephone, therefore, medical records are a useful supplemental source.

This analysis from the ongoing project is restricted to women in the catchment area of NHC who are aged 18-39 with a reported case of CIN2+/AIS from January 1, 2008 to December 31, 2010. Because some women have more than one report during this time, the first diagnostic report of the highest grade lesion was selected for this analysis.

Specimen Selection and Processing

Histopathology specimens of CIN2+ cases in New Haven County were requested from each laboratory. Of 2,223 reported cases, 1,807 (81.3%) cases were eligible for specimens to be requested. Of the specimens eligible for request, 1,572 (87%) were requested from pathology laboratories and the remaining 234 (13%) were not requested primarily due to a 12-month waiting period at a large pathology laboratory and small laboratories where specimens are not requested as often. Of the 1,572 requested, the CT HPV-IMPACT site received 1,076 (68.4%) specimens; the remainder are still pending (20.8%) or were deemed to have an insufficient amount of specimen to provide (10.8%). All of the specimens that were received were sent to the CDC for HPV typing. Of the 1,076 sent to the CDC, 919 (85.4%) were typed and 157 (14.6%) are pending. Two of the 919 typed specimens were removed from the dataset because of duplication or because the case did not live in NHC.

Blocks representative of the highest grade lesion were chosen for type-specific HPV DNA testing. Specimens were prepared at either the diagnostic laboratory of record or at Yale's pathology laboratory and included preparing serial sections of the tissue block. First and last sections were stained with hematoxylin and eosin (H&E) and two intervening 10-micron unstained sections were placed in sterile microfuge tubes for extraction[18]. After properly labeling all slides and tubes, specimens were sent to the CDC for typing and typing tests were performed on specimens for which the diagnosis could be confirmed and contained sufficient material for typing.

HPV Typing Procedures

HPV typing procedures have been previously described [18]. Briefly, DNA from sectioned blocks was extracted and tested immediately or stored at -20°C. Extracts were used in L1 consensus PCR (Roche Linear Array Assay, 450 bp amplicon). The LA assay uses HPV L1 consensus PCR with biotinylated PGMY09/11 primer sets and β-globin as an internal control for sample amplification. All samples were hybridized to the typing strip that included probes for 37 HPV types (6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 42, 45, 51, XR(52), 53, 54, 55, 56, 58, 59, 61, 62, 64, 66, 67, 68, 69, 70, 71, 72, 73, 81, 82, 83, 84, 89, IS39). Samples positive for the XR probe on the LA HPV strip that were also positive for HPV33, 35 and 58 required further evaluation to confirm or exclude the presence of HPV52. An HPV52 quantitative PCR was used to determine the status of HPV52 in these cases. Samples negative for HPV were retested with another L1 consensus PCR system. The LiPA assay uses SPF10 primers and detects 28 HPV types (6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 43, 44, 45, 51, 52, 53, 54, 56, 58, 59, 66, 68, 69, 70, 71, 73, 74, 81, 82). Samples negative for both the genomic control probe and HPV were considered inadequate for evaluation.

Geocoding and area-based poverty, race, ethnicity measures

Using patient residential addresses obtained from pathology reports, cases were geocoded to the census tract level, which is the recommended area unit of measurement when examining health disparities using area-based SES measures [17, 19]. Census tracts are small, relatively permanent subdivisions of counties that are specifically designed to be homogenous with respect to population characteristics, economic status, and living conditions and usually have between 2,500 and 8,000 residents [20]. The US Census 2006-2010 ACS 5-year estimates were used to

determine census tract sociodemographic statistics and included poverty, race and ethnicity measurements. Poverty was measured by percentage of population living below the federal poverty level, which is determined by household income, family size, and composition. Race was measured as percentage of the population that was black and ethnicity was measured as percentage of the population that was Hispanic. For each of these area-based measurements, the following cut points were used: <5.0%, 5.0-9.9%, 10.0-19.9%, and ≥ 20%. These cut points have been utilized by previous area-based CT HPV-IMPACT studies and are the cut-points recommended by the Public Health Disparities Geocoding Project for census tract poverty-level analysis [17, 21, 22].

Statistical Methods

Comparison of women with and without HPV typing data was done using Pearson's chi-square test for independence evaluating various characteristic differences. Among those who had valid typing results, chi-square test for independence was used to evaluate differences between individual level variables and the primary outcome, which was having vaccine type HPV (16 and/or 18 with or without another type) or having non-vaccine type HPV (anything other than HPV 16 or 18). Individual information was collected from the best data available including a combination of chart reviews and interviews. The Cochran-Armitage test for trend was used to evaluate if a statistically significant gradient existed by levels of the area-based measures. Trend analysis was appropriate for these measures because categories were listed in increasing proportions.

The selected variables included area-based measurements of proportion of population black, proportion of population Hispanic, and proportion of population living below federal

poverty level. Individual level variables included age, race/ethnicity, insurance, diagnosis, and diagnosis year. Age was grouped into 5 different categories based in part on recent guidelines recommending initial Pap smear screening at age 21 years and included 18-20, 21-24, 25-29, 30-34, and 35-39 years. The individual level race/ethnicity characteristic was separated into 5 categories: non-Hispanic white, non-Hispanic black, Hispanic, other, and unknown. The category "other" included American Indian, Asian, multiple, and "other" races. These races were combined into one category because of small numbers of women. Insurance was comprised of private insurance, (including HMO/PPO/Managed Care/VA insurances), public insurance (including Medicare/Medicaid), and no insurance (including women who self-paid or had no insurance). Diagnosis was comprised of 5 categories of increasing severity including CIN2, CIN2/3 (i.e., grade not specified), CIN3, AIS, and AIS+CIN. Diagnosis year includes the first three years that the program has been active (2008, 2009, 2010) and represents the year that the first diagnostic report for a case was received.

The prevalence of selected HPV types (16, 18, 31, 35, 45, 51, 52, and 58) by race and ethnicity was completed using adjusted, race-specific denominators that accounted for women with multiple HPV types. For example, a white woman infected with 2 HPV types would be counted twice for the white-specific denominator. These types were chosen either due to their respective prevalence within our data (e.g., sufficient sample size) or due to implications from the literature that racial and ethnic disparities may exist [6, 18].

Unadjusted and adjusted odds ratios and 95% confidence intervals were calculated for all variables. The generalized estimating equation (GEE) was used to calculate unadjusted odds ratios for all area-based measures to account for correlations within census tracts and logistic regression was used to calculate all individual level variables. The adjusted odds ratios represent

a full model including all variables and was calculated using GEE. SAS (v 9.2, SAS Institute, Cary, NC, 2002) was used to complete all statistical analyses.

Results

From 2008-2010, a total of 1,804 New Haven County women aged 18-39 diagnosed with CIN2+ were reported to the HPV-IMPACT monitoring system at the Connecticut site. Of these 1,804 women, 917 of them had HPV typing completed. A total of 887 did not have HPV typing results available because specimens had not been requested from pathology labs (n=234, 26.4%), requests were still pending from pathology labs (n=327, 36.9%), pathology labs deemed specimens insufficient (n=169, 19.0%) or specimen typing results were still pending at the CDC (n=157, 17.7%). CIN2+ cases with HPV DNA typing were not similar to cases without typing with respect to all demographic characteristics. Women with typing data were more likely to be 18-20 years and less likely to be 35-39 years. They were more likely to be white or Hispanic and less likely to be black. They were more likely to have a CIN 3 diagnosis and less likely to have a CIN 2 diagnosis. Finally, they were more likely to be diagnosed with CIN2+ in 2008 and less likely to be diagnosed in 2010 compared to women without typing data. However, with the exception of year, the magnitudes of these differences were not large.

Table 2 presents all of the detected HPV types in eight mutually exclusive categories. Of the 917 women who had specimens typed, HPV DNA was not detected in specimens for 47 women (5.1%). A total of 275 women (30%) had a single infection of HPV 16; 29 women (3.2%) had a single infection of HPV 18; and only one woman had a co-infection with types 16 and 18. Women with one or more non-vaccine HPV types made up 53% of the sample (n=486).

Graph 1 presents the specific HPV type prevalence among our sample size. The top 5 types with the highest prevalence were 16 (37.7%), 31 (11.6%), 52 (10.8%), 51 (9.8%), and 35 (6.0%).

Table 3 presents the percentage of cases with each characteristic by vaccine-type HPV versus non-vaccine type HPV and includes unadjusted and adjusted odds ratios with 95% confidence intervals. For the area-based measure of proportion of the population living below the federal poverty level, a significant trend existed (p=0.05). As the proportion of poverty increased, the percentage of women with non-vaccine type HPV increased and the percentage of women with vaccine type HPV decreased. This same trend existed at a nearly statistically significant level for the variables proportion population black (p=0.11) or Hispanic (p=0.06). For these area-based variables, results show that women who live in areas with higher proportions of the population black or Hispanic (≥20%) have higher percentages of non-vaccine type than vaccine type HPV. In categories with the lowest proportions of population black, Hispanic, or living below poverty level (<5%), vaccine type and non-vaccine type HPV occur at about 50% each. For individual level characteristics, the percentage of those with HPV vaccine types differed by age, race/ethnicity, and diagnosis at statistically significant levels. A higher percentage of women with CIN2 had non-vaccine type HPV (64.5%) compared to vaccine type (35.5%), while vaccine type HPV accounted for all AIS cases and a larger proportion of CIN3 diagnoses (59.5% vs. 40.5%). Women aged 21-29 years made up the majority of the sample for both vaccine type (64.3%) and non-vaccine type HPV (53.9%). Among women aged 18-20 years, a larger proportion of non-vaccine type HPV (64.0%) was discovered compared to vaccine type HPV (36.1%). The same trend existed for women 21-24, but changed among women 25-29 years with 51.4% vaccine type HPV. Women 30-34 and 35-39 years had significantly more non-vaccine HPV. Among white women there was nearly a 50% split between those who had vaccine

type and those who did not. Black women had a higher percentage of non-vaccine type HPV (63.8%) than vaccine type (36.2%). Hispanic women also had higher percentages of non-vaccine type HPV (61.2%).

Unadjusted odds ratios for all variables followed the same trends given by chi-square analyses, while the adjusted odds ratio for proportion population black revealed a significant reverse association between the variable and vaccine type HPV. Results showed the adjusted odds ratios predicting vaccine type HPV increased when the proportion of population black increased.

Table 4 shows HPV type prevalence by race and ethnicity. Specific type distribution by race/ethnicity revealed that HPV type 16 accounted for 37.6%, 26.8%, and 26.5% of types found in white, black, and Hispanic women. HPV type 35 accounted for 3.5%, 10.7%, and 6.5% of all infections for each respective race or ethnicity. HPV type 58 accounted for 2.6%, 13.4%, and 6.5% of all infections for each respective race or ethnicity. Together, non-vaccine types 35, 52, and 58 accounted for 35.8% of the HPV found among black women, 23.3% of HPV among Hispanic women and 14.8% of HPV among white women.

Discussion

This analysis expands the current literature on the distribution of HPV types among women of different SES backgrounds as well as adds to the general knowledge about HPV types found in precancerous lesions CIN2+. Analyzing the distribution of HPV types by SES factors is important in determining the prevention potential of the current HPV vaccines and monitoring the impact as well as helping to pinpoint SES disparities that confer elevated risks for HPV types not covered by the current vaccine. This is an important public health issue because disparate HPV type distribution means that certain populations of women are less likely to be protected

against cervical cancer and precursors given the current HPV types included in the bivalent and quadrivalent vaccines.

An intriguing result from this study is the difference in distribution of vaccine type HPV by individual and area-based measures of race/ethnicity. Results show that non-Hispanic black and Hispanic women are less likely to have vaccine type HPV (16/18) and more likely to have non-vaccine type HPV. This is also reflected in the area-based results of proportion population Hispanic and black. The individual level results are corroborated by the five site HPV-IMPACT analysis conducted by Centers for Disease Control [18], which examined HPV type and socioeconomic disparities at the individual level. The CDC investigation found similar disparate results showing that black and Hispanic women were less likely to have HPV 16/18. Our analysis is different because it included area-based characteristics, including poverty, as well as individual characteristics to analyze racial and ethnic disparities of HPV distribution. Both individual race/ethnicity and area-based levels of measurement show similar trends, although the area-based measure of poverty was the only significant variable. Proportion population Hispanic and black were not significant, but had clear increasing trends of non-vaccine type HPV as proportion population went from <5% black (53.8%) or Hispanic (51.6%) to >20% black (60.3%) or Hispanic (57.4%).

A puzzling finding occurred for proportion population black when all variables were included in an adjusted GEE model. The results were opposite from the unadjusted results found in chi-square and odds ratio analysis. When the variable is included in a model on its own, odds ratios show a general decrease in risk of having vaccine type HPV as proportion population black increased. However, when the full model including all variables was examined, the area-based race variable predicted an increasing risk for vaccine type HPV as proportion population

black increased. This was the only variable in the full model that gave significantly different results from what was seen in the unadjusted models. The reason for this result is unclear and warrants further investigation. The proportion population Hispanic may be influencing this result. It is possible that there is negative confounding that could be further explored in a stratified analysis.

The results suggest that HPV types not covered by the vaccine are causing a significant proportion of precancerous lesions among racial and ethnic minorities adding to the various factors responsible for cervical cancer disparities in the United States. Furthermore, the CDC study also found more HPV35 and 58 in non-Hispanic blacks and HPV45 in Hispanics compared to non-Hispanic whites [18]. This finding was also true for the type distribution among the women in our sample. However, this is not surprising because the data used in this analysis was a subset of data used in the CDC analysis. Non-vaccine types 35, 52, and 58 (all found in the top 6 most prevalent types of the study) together accounted for 35.8% of the HPV found among the black sample, 23.3% of HPV among the Hispanic sample yet only 14.8% of HPV among the white sample. Worldwide studies on HPV type distribution show that other HPV types, such as 35 and 58 in Africa, are responsible for a higher proportion of high-grade lesions than in North America and Europe [6]. Another study showed that women in sub-Saharan Africa were less likely to be infected with HPV16 than women in Europe and were more likely to have other high-risk HPV type infections [23]. These circulating types appear to be significant contributors to high-grade lesion morbidity among minority women in the United States.

The new 9-valent HPV vaccine developed by Merck is currently in phase III trials and protects against HPV types included in the current quadrivalent vaccine and additional types that this analysis implicates as producing a large proportion of precancerous lesions among minority

women. The new HPV types that the vaccine will cover are -31, -33, -45, -52, and -58. This analysis shows that the inclusion of types 52 and 58 would aid in reducing cervical lesions among minority women who receive the vaccine. However, according to this analysis and the CDC analysis, the exclusion of type 35 may produce disparate distributions yet again [18]. The results of this analysis show that type 35 is responsible for 3.5%, 10.7%, and 6.5% of HPV infection among white, black and Hispanic women respectively. Although Guan et al. suggest that type 35 has lower levels of carcinogenicity, they also show that this type is responsible for a large proportion of high-grade lesions in Africa [6]. However, the results from this study do suggest that type 35 could be an important type that is being overlooked.

Many of the results of this evaluation are consistent with the current literature showing that HPV 16 and 18 are responsible for the majority of higher grade lesions and AIS [6, 9, 23]. As expected, of the 4 women with reports of AIS, 3 tested positive for HPV 18 only and 1 tested positive for type 18 plus one or more other non-vaccine type HPV. More vaccine type HPV was found in diagnoses more advanced than CIN2, while the opposite was true for CIN2 diagnoses.

This analysis had several limitations. First, women who had typing data available were significantly different from women without typing data for all characteristics. However, specimens sent for typing were not selected based on personal characteristics of the cases thus any difference between groups should not be systematic. Second, only about half of the reported cases had typing data available due to the fact that samples are typed based on convenience of availability in this routine public health surveillance activity. Thus, the cases who have yet to be typed may contribute different results than the typed cases used in this analysis. Third, it is possible that some of the cases in our study received one of the available HPV vaccines that have been available since 2006, affecting the typing results. Fourth, we use the term “vaccine-type

HPV" to mean HPV 16 and/or 18 with or without any other HPV type. Since some cases had HPV16 and/or 18 accompanied by one or more non-vaccine type HPV (20.6% of cases with vaccine type HPV) it is impossible to definitively parse out which type was responsible for the cervical lesions. However, some research shows the synergistic effect of having multiple HPV infections especially when one of the types consists of 16 or 18 [24]. Finally, this analysis may not generalize beyond New Haven County, Connecticut. However, NHC has comparable proportion statistics to the rest of the United States for race and ethnicity categories of black, white, and Hispanic/Latino. NHC had 1.4% higher white population, a 1.3% lower Hispanic population and a 0.01% higher black population compared to the United States. NHC is more comparable to the United States in terms of race and ethnicity than Connecticut as a whole [25]. Furthermore, a strength of this analysis is the high case ascertainment and therefore large sample size achieved within the NHC catchment area due to the mandatory reporting of CIN2+ and the cooperation of pathology laboratories, which limits selection bias and strengthens the internal validity of the study.

This study adds to the available baseline data on HPV type prevalence in order to aid in measuring the wide-scale impact of the HPV vaccine in the next decade. This analysis suggests that non-vaccine type HPV is an important contributing factor for high-grade lesions among women of different racial and ethnic backgrounds. This analysis also may help inform future multivalent HPV vaccine development endeavors that may be key to decreasing racial and ethnic cervical lesion and cancer disparities.

Future Implications

This analysis will aid future interpretations of surveillance data regarding impact of vaccination given that certain HPV types seem to be more prevalent among different race/ethnic

groups. HPV types not included in the current vaccines are causing a significant amount of precancerous lesion morbidity among minority women and should be considered for future multi-valent HPV vaccines that will "level the playing field" in terms of risk among different races and ethnicities. Area-based as well as individual characteristics seem to be important in determining risk for acquiring vaccine type HPV and therefore should be considered for future analyses monitoring vaccine impact. Furthermore, the different results in unadjusted and adjusted models suggest a complex interplay between individual and area based measurements that warrant further investigation. Area-based measurements may contribute new and different data compared to individual measurements of race and ethnicity that can help parse out individual risk factors compared to broader social and environmental risk factors.

Table 1. HPV typed samples versus not typed samples among women aged 18-39 years with CIN2+ reports during 2008-2010 by selected characteristics.

	NHC Women with CIN2+ Reports (Total=1804)		
Characteristic	Typed N = 917 (50.8)	Not Typed N = 887 (49.2)	p-value
Age			0.016
18-20	91 (9.9)	50 (5.6)	
21-24	260 (28.4)	253 (28.5)	
25-29	275 (30.0)	283 (31.9)	
30-34	179 (19.5)	177 (20.0)	
35-39	112 (12.2)	124 (14.0)	
Race/Ethnicity			<0.001
NH White	474 (51.7)	373 (42.1)	
NH Black	96 (10.5)	110 (12.4)	
Hispanic	153 (16.7)	133 (15.0)	
Other	41 (4.5)	39 (4.4)	
Unknown	153 (16.7)	232 (26.2)	
Insurance			<0.001
Private	588 (65.5)	486 (57.0)	
Public	289 (32.2)	322 (37.8)	
No Insurance	18 (2)	36 (4.2)	
Other	3 (0.3)	8 (0.9)	
Diagnosis			0.02
CIN 2	580 (63.3)	614 (69.2)	
CIN 2/3	130 (14.2)	89 (10.0)	
CIN 3	201 (21.3)	179 (20.2)	
AIS	4 (0.4)	5 (0.6)	
AIS+CIN	2 (0.2)	0 (0.0)	
Diagnosis Year			<0.001
2008	509 (55.5)	161 (18.15)	
2009	297 (32.4)	288 (32.5)	
2010	111 (12.1)	438 (49.4)	

Table 2. HPV Type Count and Percentage

HPV Type	
16 only	275 (30.0)
16+18 only	1 (0.1)
16+ any non vacc. type	66 (7.2)
18 only	29 (3.2)
18+ any non vacc. type	9 (1.0)
16+18+ any non vacc. type	4 (0.4)
Non vacc. type only	486 (53.0)
No type	47 (5.1)
Total	917

Table 3. HPV Type by Area-Based and Individual Level Characteristics

	HPV Type			Generalized Estimated Equation	
Characteristic	Vaccine N=(384)	Non-Vaccine N=(486)	p-value	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Proportion pop. black			0.11*		
<5.0	178 (46.2)	207 (53.8)		1	1
5.0-9.9	45 (47.9)	49 (52.1)		1.02 (0.91, 1.14)	1.09 (0.98. 1.22)
10.0-19.9	69 (43.4)	90 (56.6)		0.97 (0.88, 1.07)	1.11 (1.0, 1.24)
≥ 20	92(39.7)	140 (60.3)		0.94 (0.87, 1.01)	1.12 (1.01, 1.25)
Proportion pop. Hispanic			0.06*		
<5.0	104 (48.4)	111 (51.6)		1	1
5.0-9.9	117 (48.2)	126 (51.9)		1.0 (0.91, 1.09)	0.98 (0.89, 1.08)
10.0-19.9	68 (36.0)	121 (64.0)		0.88 (0.80, 0.97)	0.86 (0.77, 0.96)
≥ 20	95 (42.6)	128 (57.4)		0.94 (0.86, 1.03)	0.97 (0.85, 1.10)
Proportion pop. living below federal poverty level			0.05*		
<5.0	139 (49.5)	142 (50.5)		1	1
5.0-9.9	90 (42.5)	122 (57.6)		0.93 (0.85,1.02)	0.97 (0.89, 1.06)
10.0-19.9	84 (42.0)	116 (58.0)		0.93 (0.85, 1.01)	0.93 (0.83, 1.03)
≥ 20	71 (40.1)	106 (59.9)		0.91 (0.83, 1.0)	0.89 (0.78, 1.02)
Age			0.02		
18-20	31 (36.1)	55 (64.0)		0.81 (0.45, 1.46)	1.0 (0.88, 1.14)
21-24	115 (45.6)	137 (54.4)		1.21 (0.76, 1.92)	1.09 (0.97, 1.22)
25-29	132 (51.4)	125 (48.6)		1.52 (0.96, 2.4)	1.13 (1.0, 1.28)
30-34	63 (37.1)	107 (62.9)		0.85 (0.52, 1.40)	0.98 (0.86, 1.11)
35-39	43 (41.0)	62 (59.1)		1	1
Race/Ethnicity			0.01		
White	224 (50.1)	223 (48.9)		1	1
Black	34 (36.2)	60 (63.8)		0.56 (0.36, 0.89)	0.91 (0.80, 1.04)
Hispanic	57 (38.8)	90 (61.2)		0.63 (0.43, 0.92)	0.91 (0.82, 1.0)
Other	13 (33.3)	26 (66.7)		0.50 (0.25, 0.99)	0.90 (0.77, 1.06)
Unknown	56 (39.2)	87 (60.8)		0.64 (0.44, 0.94)	0.92 (0.82, 1.03)
Insurance			0.45		
Private	248 (44.6)	308 (55.4)		1	1
Public	122 (44.5)	152 (55.5)		1.0 (0.75, 1.33)	1.0 (0.93, 1.08
No Insurance	7 (38.9)	11 (61.1)		0.79 (0.30, 2.07)	1.01 (0.77, 1.33)
Other	0 (0.0)	3 (100.0)		<.01 (<.01, >999.99)	0.57 (0.51, 0.66)
Diagnosis			<0.001		
CIN 2	193 (35.5)	350 (64.5)		1	1
CIN 2/3	69 (54.8)	57 (45.2)		2.20 (1.48, 3.25)	1.23 (1.12, 1.35)
CIN 3	116 (59.5)	79 (40.5)		2.66 (1.90, 3.73)	1.30 (1.17, 1.36)
AIS	4 (100.0)	0 (0.0)		>999.99 (<.01, >999.99)	1.92 (1.70, 2.17)
AIS+CIN	2 (100.0)	0 (0.0)		>999.99 (<.01, >999.99)	1.91 (1.54, 2.37)
Diagnosis Year			0.55		
2008	219 (45.1)	267 (54.9)		1	1

2009	116 (41.6)	163 (58.4)	0.87 (0.64, 1.17)	0.97 (0.91, 1.04)
2010	49 (46.7)	56 (53.3)	1.07 (0.70, 1.63)	1.0 (0.90, 1.11)

*P-values for area-based measures were obtained using the chi-square statistic for trend

Figure 1.

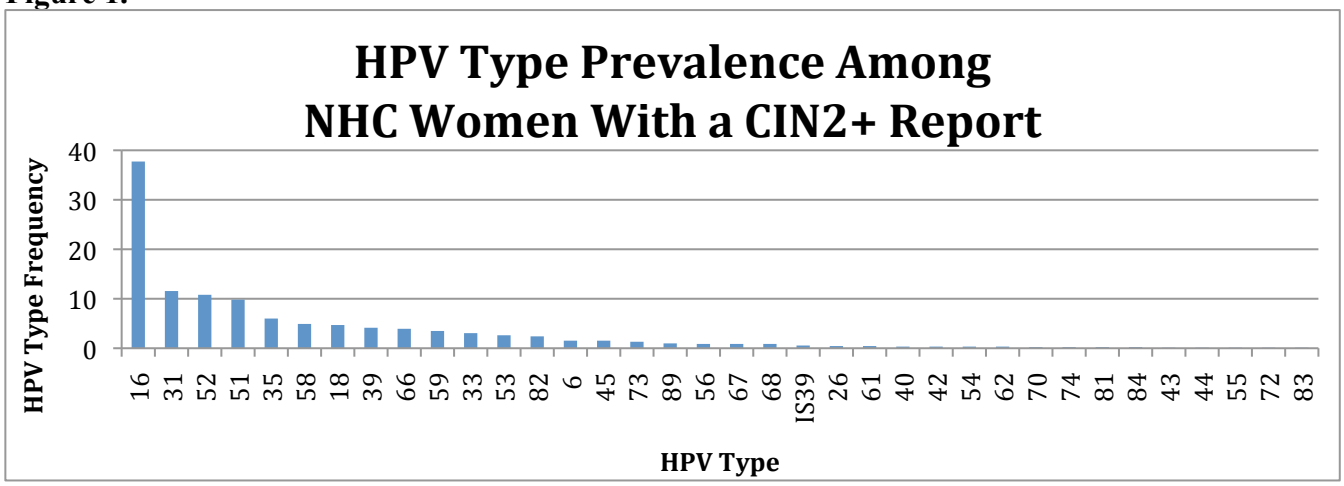
HPV Type Prevalence Among
NHC Women With a CIN2+ Report
HPV Type Frequency
40
30
20
10
0
16
31
52
51
35
58
18
39
66
59
33
53
82
6
45
73
89
56
67
68
IS39
26
61
40
42
54
62
70
74
81
84
43
44
55
72
83
HPV Type

Table 4. Percentage of HPV Type Found Among Women of Selected Race/Ethnicities

	16	18	31	35	45	51	52	58
Race/Ethnicity								
White	37.6	4.1	10.5	3.5	1.1	9.2	8.7	2.6
Black	26.8	4.5	0.9	10.7	1.8	7.1	11.6	13.4
Hispanic	26.5	4.9	10.8	6.5	2.2	7.0	10.3	6.5

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